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Optical coherence tomography can monitor reversible nerve-fibre layer changes in a patient with ethambutol-induced optic neuropathy

Ethambutol (EMB) has been used as an antimycobacterial agent against tuberculosis since 1961, and its principal side effect is toxic optic neuropathy, which can be seen in up to 6% of patients.[1 2]

Through the use of optical coherence tomography (OCT), we can document evidence of reversible changes in nerve-fibre layer (NFL) secondary to EMB-induced optic neuropathy.

Case report

A 70-year-old man weighing 70 kg, who was being treated for *Mycobacterium avium intracellulare* complex pneumonia, initially presented with a 3-month history of gradual, painless loss of vision in both eyes. He had received EMB treatment for 7 months at 2 g/day (29 mg/kg/day). His visual complaints began 7 months after initiation of EMB treatment, and continued to worsen up to his presentation to our clinic. Before EMB treatment, his best-corrected vision was 20/30 OU (with mild nuclear sclerotic cataracts), but with normal subjective colour and contrast sensitivity.

Our patient underwent a full neuro-ophthalmological examination, which included an assessment of colour vision using the eight-plate Ishihara Color Vision Test, Humphrey Field Analyzer (HFA) 30-2 (SITA Fast test, Humphrey-Zeiss Medical Systems, Dublin, California, USA), and contrast sensitivity using the Vision Contrast Test System (Vistech, Dayton, Ohio, USA). In addition, OCT (OCT 3000, Humphrey-Zeiss) was performed on both eyes of the patient. All quantitative measurements were obtained by OCT using the retinal NFL (RNFL) analysis protocol (Stratus OCT 3). The basic principles and technical characteristics of the OCT have been described previously.[3 4]

The results are presented categorised by the clinical tests performed. The patient visits are abbreviated as A for the initial visit (3 months after discontinuing a 7-month regimen of EMB), B for the second visit (5 months after discontinuing EMB) and C for the third visit (8 months after discontinuing EMB).

Humphrey visual field analysis

The patient presented with a new superior visual field (VF) defect in his right eye during visit B. By the third visit, the patient showed an improvement in his superior field VF defects when compared with his second visit. Figure 1 and table 1 give more detailed descriptions of the results.

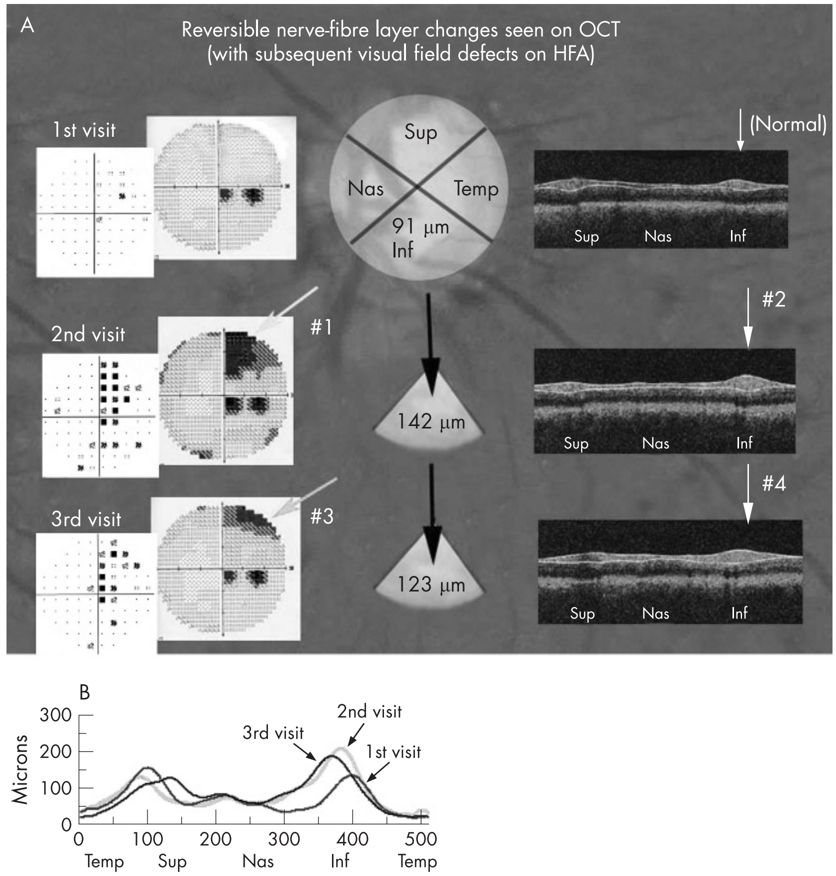

Figure 1 (A) There is a new onset superior–temporal visual field (VF) defect on Humphrey VF analysis (HFA) mean deviation (MD) and pattern standard deviation (PSD) plots observed on second visit, arrow #1. This corresponds well with increased nerve-fibre layer (NFL) thickness secondary to axonal swelling in the inferior layer on optical coherence tomography (OCT), arrow #2. Subsequently, there is a clinical improvement in the superior-temporal VF defect (MD and PSD) by the third visit, arrow #3, with reversible changes in the NFL thickness on OCT, arrow #4. (B) The arrows indicate the thickness (at the three separate visits) of the retinal NFL (RNFL) along the temporal–superior–nasal–inferior–temporal (temp–sup–nasal–inf–temp) plot provided by the OCT RNFL thickness analyser. Note the degree of thickening (axonal swelling) of the inferior quadrant RNFL by the second visit and the improvement (reversible changes) seen by the third visit.

Optical coherence tomography

OCT showed a significant increase in NFL thickness in the inferior quadrant of the right eye during visit B in comparison to visit A. This corresponded well with the HFA superior VF deficits. The average RNFL thickness of the inferior quadrant was 142 μm, ranging from a minimum 84 μm to a maximum 201 μm, or 156% thicker than the OCT data from the initial visit. We were unable to perform OCT of the left eye at this visit owing to patient non-compliance. Hence, we excluded the left eye from any further OCT or HFA analysis. By the third visit (C), OCT revealed a significant decrease in the inferior quadrant RNFL, down to an average 123 μm, or a 13.4% loss of NFL thickness when compared with the second visit, but still 135% thicker than that seen on the patient's initial presentation (fig 1).

Comment

OCT is a useful tool for examining the NFL thickness of certain optic neuropathies.[5 6] In this study, we used OCT to monitor reversible axonal swelling in a patient with EMB-induced optic neuropathy. The marked thickening of the inferior quadrant nerve fibre on OCT corresponded well with the VF defects in the superior quadrant observed on HFA. Furthermore, as the thickness of the inferior quadrant NFL decreased, we saw a concurrent improvement in the patient's VF defects within the superior quadrant. We attribute these reversible NFL changes to retinal ganglion cell axonal swelling that resolved over time after cessation of EMB.

We believe that the heavier distribution of magnocellular axons (M cells) within the peripheral RNFL may play an important role in the reversible changes in NFL that we observed. Unlike parvocellluar axons (P cells), M cells are larger, serve low spatial frequency of contrast sensitivity and motion stereopsis.[6–8] The large-calibre M cell axons fire (neuronal activity/second) less often owing to their transient response characteristics and hold an anatomical advantage of having more mitochondria

Table 1 Results for the subject's visual acuity, contrast sensitivity, colour vision, fundus examination, Humphrey visual field analysis and optical coherence tomography

	Visit A	Visit B	Visit C
Visual acuity (OU)	20/200 OU	20/80 OD 20/60 OS	20/60 OU
Contrast sensitivity (OD)			
High spatial frequency	No ability	No ability	No ability
Low spatial frequency	Below 10% of that observed in a normal population	Up to 70% of that observed in a normal population	Up to 90% of that observed in a normal population
Colour vision (OD)	50% error (4/8 plates correctly scored)	50% error (4/8 plates correctly scored)	50% error (4/8 plates correctly scored)
Fundus examination (OU)	Persistent temporal pallor and thin NFL		
Humphrey VF analysis	Within normal limits (MD = −0.49 dB, PSD = 1.81 dB)	Superior VF defect and OD (MD = −9 (6.24) dB, $p<0.01$, PSD = 6.61 dB, $p<0.005$)	Improved superior VF defect and OD, when compared with visit B (MD = −5.4 (3.29) dB, $p<0.01$, PSD = 3.77 dB, $p<0.02$)

MD, mean deviation; NFL, nerve fibre layer; PSD, pattern standard deviation; VF, visual field.
High spatial frequency of contrast sensitivity comprised of 12 cycles/degree and 18 cycles/degree on the Vision Contrast Test System (VCTS) chart.
Low spatial frequency of contrast sensitivity comprised of 1.5, 3, and 6 cycles/degree on the VCTS chart. The Humphrey VF analysis was performed on the right eye.

because of their larger volume in comparison to P cells.[6–9] It is reasonable to suggest that the reversible axonal changes we observed within the peripheral RNFL were due to a significant recovery of the retinal ganglion cells, most notably M cells, after the cessation of EMB.

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Frequency of retinal macroaneurysms in adult Chinese: the Beijing Eye Study

A retinal arterial macroaneurysm is an acquired retinal vascular abnormality, typically a solitary, round or fusiform aneurysm arising in one of the four major branch retinal arteries in the paramacular area. According to hospital-based investigations, most patients in whom this pathological condition develops are in their sixth or seventh decade of life and have a history of systemic hypertension, ophthalmoscopic evidence of retinal arteriolar sclerosis or both. Visual loss is caused by exudation or bleeding from the aneurysm. Massive retinal bleeding from a ruptured aneurysm can be confined to the preretinal, intraretinal or subretinal space, or dispersed into the vitreous.[1–4] Since most reports on retinal macroaneurysm arise from hospital-based studies and because no information is available about the prevalence of retinal macroaneurysms, particularly in the Chinese population, this population-based study was conducted.

Case report

The Beijing Eye Study is a population-based cohort study in northern China, carried out in four communities from the Haidian urban district in the Northern part of central Beijing and in three communities from a rural district in the village area of Yufa (Daxing District) in the south of Beijing.[5] The medical ethics committee of the Beijing Tongren Hospital, Beijing, China approved the study protocol, and all participants gave informed consent, according to the Declaration of Helsinki. At the time of the survey in the year 2001, there were 5324 individuals aged ⩾40 years residing in these 7 communities. In all, 4439 individuals (2505 women) participated in the eye examination, corresponding to an overall response rate of 83.4%. This study included 8609 eyes of 4335 (97.7%) subjects for whom readable fundus photographs were available. Mean age was 56.0 (10.4) years (range 40–101 years), mean refractive error was −0.39 (2.24) D (range −20.13 to +7.50 D). The examinations performed during the study included colour photographs of the optic disc and macula.

Two retinal macroaneurysms were detected on the fundus photographs of one eye (prevalence rate per eye: 0.01% (0.01%) (mean (SE)); 95% CI 0.00% to 0.03%) of a female subject aged 67 years (prevalence rate per subject 0.02% (0.02%); 95% CI 0.00% to 0.07%). Visual acuity was hand movements due to marked macular oedema with pronounced deposition of hard exudates in the foveal region. One of the macroaneurysms was located superior to the fovea and inferior to the superior temporal vessel arcade leading to the foveal oedema; the other macroaneurysm was located nasally to the optic disc at a distance of about 1.5 mm. The intraocular pressure was 15 mm Hg. The contralateral eye showed a normal ophthalmoscopic appearance of the fundus.

Comment

The data suggest that retinal macroaneurysms may occur in about 1 of 9000 eyes or in approximately 1 of 4500 adult Chinese.

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